REMARKS

After entry of this amendment, claims 65, 67-72, 74-77, 79-83, 85-88, 90-93, 96-99, 101-106, 108-109, 111-116, and 118 will be pending in the application. Claims 65, 75, 86, 99, and 109 have been amended to more particularly point out and distinctly claim that which Applicants regard as the invention. Claims 66, 73, 78, 83, 84, 89, 94, 95, 100, 107, 110, and 117 have been canceled without prejudice to Applicants right to pursue prosecution of the claimed subject matter in related applications. The amendments are fully supported by the specification as originally filed and, as such no new matter has been added. Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application.

1. THE CLAIMS ARE NOT ANTICIPATED UNDER 35 U.S.C. § 102(b)

Claims 75-79, 84-90, 95, and 96 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gross *et al.* (U.S. Patent No. 5,848,991; "Gross"). The Examiner erroneously interprets Gross as disclosing a method of delivering various drugs and medicine intradermally using a needle with an outlet at a depth of 250 μm-2mm in a controlled manner based on needle diameter. The Examiner contends that Gross discloses that the delivery can be pulsatile, thereby anticipating claims 85 and 96 of the current application, which recite that the substance is administered by repeated bolus injection. The Examiner further contends that it is inherent in Gross that the intradermal injections will be absorbed systemically from the dermis due to the linking of the intradermal compartment to systemic circulation via blood circulation. The rejection of the claims is in error and should be withdrawn for the reasons detailed below.

Anticipation can only be established by a single prior art reference that describes *each and every element* of the claimed invention. *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q. 2d 1896 (Fed. Cir. 1991). Gross does not anticipate the claimed invention because bolus administration and the required systemic absorption profile are not disclosed, explicitly or inherently in Gross.

The amended claims relate to a method of administration of low molecular weight heparin or a dopamine receptor agonist to the intradermal compartment of a mammal's skin by *bolus administration*. In the embodiment claimed, bolus administration results in an

improved systemic absorption relative to that obtained from subcutaneous administration of the same substance.

Gross is devoid of any teaching relating to bolus delivery of substances. It is the Applicant's disclosure that teaches the parameters and significance for bolus ID administration. Bolus administration, as defined by the instant application, is intended to mean the delivery of an amount of substance within a period of less than ten (10) minutes (See, ¶ 0021 at page 9 of the Specification as filed). Delivery of a substance over a period of time that is greater than 10 minutes is defined as "infusion" (See, the instant specification at ¶ 0021, page 9)

Gross is devoid of any description of bolus administration or any description of delivering a substance over a period of time less than 10 minutes. Gross does describe delivery in a pulsatile manner, but only in the context of a continuous infusion (See Gross at Col. 4, ¶ 50-54). Delivery by infusion (*i.e.*, over 10 minutes, is opposite that of delivery by bolus, *i.e.*, under 10 minutes.

The Examiner has erroneously equated pulsatile delivery with bolus delivery. The term "pulsatile delivery" is used in the instant specification in accordance with its ordinary and customary meaning as understood by one skilled in the art *i.e.*, a delivery which is characterized by a series of intermittent rhythmic occurrences or pulses of delivery over a period of time. For example, the specification states that in the case of delivering fertility hormone for pregnancy induction, pulsatile delivery might be ideal which requires intermittent peaks every 90 minutes with total drug clearance in between pulses (*see*, instant specification at p. 11; ¶ 0023).

As Gross does not describe each and every element of the claimed invention, it cannot anticipate and the rejection should be withdrawn.

2. THE CLAIMED INVENTION IS NOT OBVIOUS OVER GROSS IN VIEW OF PURI OR D'ANTONIO

Claims 65-74, 80, 81, 83, 91, 92, 94, 99-105, 107-115, 117, and 118 stand rejected under 35 U.S.C. §103(a) as unpatentable over Gross in view of Puri *et al.*, (2000, *Vaccine*, 18:2600-12; "Puri") or U.S. Patent No. 6,056,716 to D'Antonio ("D'Antonio"). Applicants respectfully disagree with the rejection because there is no suggestion, either in the references cited by the Examiner or in the knowledge of one of ordinary skill in the art to modify the references or to combine the teachings of the references to arrive at the presently claimed

invention. In the instant case, the combination of Gross with either Puri or D'Antonio fails to suggest bolus administration to the intradermal space to achieve an improved systemic absorption profile. Applicants respectfully submit that the rejection should be withdrawn.

CONCLUSION

The Applicant respectfully requests that the Examiner enter the amendments and consider the remarks made herein. Withdrawal of all rejections, and an allowance is earnestly sought. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining items.

Respectfully submitted, by Jacqueline Bunn Reg No. 43,492

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